



General

Guideline Title

Guideline on the investigation and management of acute transfusion reactions. Prepared by the BCSH Blood Transfusion Task Force.

Bibliographic Source(s)

Tinegate H, Birchall J, Gray A, Haggas R, Massey E, Norfolk D, Pinchon D, Sewell C, Wells A, Allard S. Guideline on the investigation and management of acute transfusion reactions. Prepared by the BCSH Blood Transfusion Task Force. Br J Haematol. 2012 Oct;159(2):143-53. [36 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the quality of the evidence (A-C) and strength of recommendation (strong [grade 1], weak [grade 2]) are given at the end of the "Major Recommendations" field.

Recognition and Initial Management of Acute Transfusion Reactions

All patients should be transfused in clinical areas where they can be directly observed, and where staff are trained in the administration of blood components and the management of transfused patients, including the emergency treatment of anaphylaxis (1C).

The recognition and immediate management of acute transfusion reaction (ATR) should be incorporated into local transfusion policies and there should be mandatory transfusion training requirements for all clinical and laboratory staff involved in the transfusion process (2C).

Patients should be asked to report symptoms that develop within 24 hours of completion of the transfusion (2C).

Initial Clinical Assessment

If a patient develops new symptoms or signs during a transfusion, this should be stopped temporarily, but venous access maintained. Identification details should be checked between the patient, their identity band and the compatibility label of the blood component. Perform visual inspection of the component and assess the patient with standard observations (1C).

Severe Reactions

If a patient being transfused for haemorrhage develops hypotension, careful clinical risk assessment is required. If the hypotension is caused by haemorrhage, continuation of the transfusion may be life-saving. In contrast, if the blood component is considered the most likely cause of

hypotension, the transfusion must be stopped or switched to an alternative component and appropriate management and investigation commenced (1C).

Mild or Moderate Reactions

For patients with mild reactions, such as pyrexia (temperature of $\geq 38^{\circ}\text{C}$ AND rise of $1-2^{\circ}\text{C}$ from baseline), and/or pruritus or rash but WITHOUT other features, the transfusion may be continued with appropriate treatment and direct observation (2B).

Management of Acute Transfusion Reactions

Initial treatment of ATR is not dependent on classification but should be directed by symptoms and signs. Treatment of severe reactions should not be delayed until the results of investigations are available (1C).

Severe Reactions

Anaphylaxis should be treated with intramuscular (IM) adrenaline (epinephrine) according to United Kingdom Resuscitation Council (UKRC) guidelines. Patients who are thrombocytopenic or who have deranged coagulation should also receive IM adrenaline if they have an anaphylactic reaction (1A).

Moderate Reactions

If a patient develops sustained febrile symptoms or signs of moderate severity (temperature $\geq 39^{\circ}\text{C}$ OR a rise of $\geq 2^{\circ}\text{C}$ from baseline AND/OR systemic symptoms such as chills, rigors, myalgia, nausea or vomiting), bacterial contamination or a haemolytic reaction should be considered (1C).

Mild Reactions

Patients with mild isolated febrile reactions may be treated with oral paracetamol (500-1000 mg in adults). Patients with mild allergic reactions may be managed by slowing the transfusion and treatment with an antihistamine (2C).

Laboratory Investigation of ATR

Standard Investigations

In all moderate and severe transfusion reactions, standard investigations, including full blood count, renal and liver function tests and assessment of the urine for haemoglobin should be performed (2C).

Investigations Dependent on Symptom Complex

If febrile symptoms of moderate severity are sustained, implicated units should be returned to the laboratory for further investigation, the blood service contacted immediately so that associated components from the implicated donation can be withdrawn and the patient sampled for repeat compatibility and culture (1C).

Patients who have experienced moderate or severe allergic reactions should have immunoglobulin A (IgA) levels measured. Low levels found on screening, in the absence of generalised hypogammaglobulinaemia, should be confirmed by a more sensitive method and IgA antibodies should be checked. Patients with IgA deficiency diagnosed after an ATR should be discussed with an allergist or immunologist regarding future management (2C).

Testing the Patient for Human Leucocyte Antibodies (HLA), Human Platelet Antibodies (HPA) or Human Neutrophil-Specific Antibodies (HNA)

In the absence of platelet or granulocyte transfusion refractoriness, or acute post-transfusion thrombocytopenia or leucopenia, investigation of the patient with ATR for leucocyte, platelet or neutrophil-specific antibodies is not indicated (1B).

Subsequent Management of Patients with Repeated Reactions

Febrile Non-Haemolytic Transfusion Reactions (FNHTR)

For patients with recurrent febrile reactions, the task force recommends a trial of premedication with oral paracetamol given one hour before the reaction is anticipated (or nonsteroidal anti-inflammatory drugs in patients with predominant chills or rigors - but an assessment of the risks of medication against the severity of reaction should be made in each case). Patients who continue to react should have a trial of washed blood components (2C).

Allergic Reactions

For recurrent mild allergic reactions, there is no evidence to support routine prophylaxis with antihistamines or steroids. Alternative causes, such as allergy to drugs or latex gloves, should be excluded (2C).

For patients with recurrent moderate or severe allergic reactions, other than those in which the patient is IgA deficient, options for further transfusion include:

- Use of directly monitored transfusion of standard components in a clinical area with resuscitation facilities. Consider antihistamine prophylaxis (although the evidence for efficacy is low, the risks are also low). This may be the only option when further transfusion is urgent and withholding blood is a greater risk (2C).
- Transfusion of washed red cells or platelets (2C).
- The use of pooled solvent-detergent treated fresh frozen plasma (FFP) when there are recurrent allergic reactions to FFP in patients undergoing plasma exchange (2B).

Patients who have experienced an anaphylactic reaction associated with transfusion must be discussed with an allergist or immunologist, in keeping with UKRC guidelines (1C).

Patients with IgA Deficiency

Patients with confirmed IgA deficiency and a history of reaction to blood should be transfused with components from IgA-deficient donors (first choice) or washed red cells (second choice) if time allows (1C).

Life-saving transfusion should not be denied or delayed if these are not immediately available but the facilities and skills to manage severe allergic reactions must be present (1C).

Patients with known IgA deficiency (IgA <0.07g/l) and no history of reactions to blood must be assessed on an individual basis, taking into account the urgency of transfusion, the indication for IgA testing, the anticipated frequency of transfusion, and history of allergy/anaphylaxis in other settings. Most will receive standard components without problems, but discussion with a transfusion medicine or clinical immunology or allergy specialist is advisable if time allows (2C).

Reporting ATR

All transfusion reactions except mild febrile and/or allergic reactions must be reported to appropriate regulatory and haemovigilance organisations (Medicines and Healthcare Products Regulatory Agency [MHRA] and Serious Hazards of Transfusions [SHOT]) and should also be reviewed within the hospital (1C).

Definitions:

Quality of Evidence

(A) High: Further research is very unlikely to change confidence in the estimate of effect. Current evidence derived from randomised clinical trials without important limitations.

(B) Moderate: Further research may well have an important impact on confidence in the estimate of effect and may change the estimate. Current evidence derived from randomised clinical trials with important limitations (e.g., inconsistent results, imprecision – wide confidence intervals or methodological flaws – e.g., lack of blinding, large losses to follow up, failure to adhere to intention to treat analysis), or very strong evidence from observational studies or case series (e.g., large or very large and consistent estimates of the magnitude of a treatment effect or demonstration of a dose-response gradient).

(C) Low: Further research is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. Current evidence from observational studies, case series or just opinion.

Strength of Recommendations

Strong (grade 1): Strong recommendations (grade 1) are made when there is confidence that the benefits do or do not outweigh harm and burden. Grade 1 recommendations can be applied uniformly to most patients. Regard as 'recommend'.

Weak (grade 2): Where the magnitude of benefit or not is less certain a weaker grade 2 recommendation is made. Grade 2 recommendations require judicious application to individual patients. Regard as 'suggest'.

Clinical Algorithm(s)

The original guideline document contains a flow diagram for recognition and initial management of suspected acute transfusion reactions.

Scope

Disease/Condition(s)

Acute transfusion reactions

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Allergy and Immunology

Critical Care

Emergency Medicine

Hematology

Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Clinical Laboratory Personnel

Hospitals

Nurses

Physicians

Public Health Departments

Guideline Objective(s)

To provide clear guidance for United Kingdom (UK) practitioners on the recognition, investigation and management of acute adverse reactions to blood components

- To provide a flow diagram to aid recognition of acute transfusion reactions and their immediate clinical management
- To advise on further management of the patient during the reaction
- To provide advice on the use of investigations
- To discuss management of subsequent transfusions
- To present recommendations for reporting adverse reactions to UK haemovigilance organisations, to blood services, and within the hospital

Target Population

All patients developing adverse symptoms and signs related to blood or blood component transfusion

Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

1. Recognition and immediate management of signs and symptoms of acute transfusion reactions
2. Careful clinical risk assessment of hypotension
3. Standard investigations, including full blood count, renal and liver function tests and assessment of the urine for haemoglobin
4. Measuring immunoglobulin A (IgA) levels
5. Testing for human leucocyte antibodies (HLA), human platelet antibodies (HPA), or human neutrophil-specific antibodies (HNA) (not generally indicated)

Treatment/Management/Prevention

1. Discontinuation of transfusion
2. Intramuscular (IM) adrenaline (epinephrine) for severe anaphylaxis
3. Consideration of bacterial contamination or a haemolytic reaction if fever or other moderate symptoms are present
4. Oral paracetamol for mild allergic reactions
5. Slowing the transfusion and treatment with an antihistamine for mild allergic reactions
6. Returning implicated blood components units to the laboratory for further investigation
7. Premedication with oral paracetamol or nonsteroidal anti-inflammatory drugs in patients with recurrent febrile reactions
8. Routine prophylaxis with antihistamines or steroids in patients with recurrent mild allergic reactions (not recommended)
9. Use of directly monitored transfusion of standard components in a clinical area with resuscitation facilities
10. Antihistamine prophylaxis in patients with recurrent severe reactions
11. Transfusion of washed red cells or platelets
12. Use of pooled solvent-detergent treated fresh frozen plasma (FFP) when there are recurrent allergic reactions to FFP in patients undergoing plasma exchange
13. Management of patients with known IgA deficiency
14. Reporting acute transfusion reactions to appropriate regulatory and haemovigilance organisations

Major Outcomes Considered

- Signs and symptoms of acute transfusion reactions (ATRs)
- Effectiveness of interventions in management and prevention of ATRs

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

With the assistance of the Oxford Systematic Reviews Initiative (SRI), the following databases were searched for relevant publications in English: MEDLINE (from 1950), EMBASE (from 1980), CINAHL (from 1982), The Cochrane Library, DARE (CRD website) and SRI handsearch databases. The initial search and filtering produced 1080 systematic reviews and randomised controlled trials and 878 observational studies from which relevant publications were extracted by the members of the Writing Group.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

The quality of evidence is graded as high (A), moderate (B) or low (C). To put this in context it is useful to consider the uncertainty of knowledge and whether further research could change what is known or is certain.

(A) High: Further research is very unlikely to change confidence in the estimate of effect. Current evidence derived from randomised clinical trials without important limitations.

(B) Moderate: Further research may well have an important impact on confidence in the estimate of effect and may change the estimate. Current evidence derived from randomised clinical trials with important limitations (e.g., inconsistent results, imprecision – wide confidence intervals or methodological flaws – e.g., lack of blinding, large losses to follow up, failure to adhere to intention to treat analysis), or very strong evidence from observational studies or case series (e.g., large or very large and consistent estimates of the magnitude of a treatment effect or demonstration of a dose-response gradient).

(C) Low: Further research is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. Current evidence from observational studies, case series or just opinion.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to quote levels of evidence (see the "Rating Scheme for the Strength of Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The guideline group was selected to be representative of United Kingdom-based medical experts.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Strong (grade 1): Strong recommendations (grade 1) are made when there is confidence that the benefits do or do not outweigh harm and burden. Grade 1 recommendations can be applied uniformly to most patients. Regard as 'recommend'.

Weak (grade 2): Where the magnitude of benefit or not is less certain a weaker grade 2 recommendation is made. Grade 2 recommendations require judicious application to individual patients. Regard as 'suggest'.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate investigation, specific treatment and prevention, where possible, of future episodes for acute transfusion reactions

Potential Harms

- Caution would be required in the use of non-steroidal anti-inflammatory drugs in patients with thrombocytopenia or reduced platelet function. An assessment of the risks of medication against the severity of reaction should be made in each case.
- If the presumed acute transfusion reaction (ATR) is severe or life-threatening, a doctor should be called immediately and the blood transfusion discontinued. Caution is required in bleeding patients where hypotension may be associated with haemorrhage and continuing the transfusion may be life-saving.

Qualifying Statements

Qualifying Statements

While the advice and information in these guidelines are believed to be true and accurate at the time of going to press, neither the authors, the British Society for Haematology nor the publishers accept any legal responsibility for the content of the guidelines.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Safety

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Oct

Guideline Developer(s)

Source(s) of Funding

British Committee for Standards in Haematology

Guideline Committee

British Committee for Standards in Haematology Blood Transfusion Task Force

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [British Journal of Haematology Web site](#) .

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on January 15, 2013. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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